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Client Alert Commentary

Latham & Watkins Healthcare & Life Sciences Practice October 25, 2023 | Number 3181

Recent FDA Guidance Signals Increased Willingness to Engage Industry Stakeholders

The Agency's recent draft guidance document on formal meetings with PDUFA product sponsors and applicants could increase opportunities for interactions between FDA and industry stakeholders.

On September 22, 2023, the US Food and Drug Administration (FDA or the Agency) released a draft guidance titled "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products" (the Draft Guidance).[1] The Draft Guidance includes two new types of formal meetings to which FDA committed during user fee reauthorization negotiations that led to the Prescription Drug User Fee Act (PDUFA) VII.[2]

The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) collaborated in producing the Draft Guidance.[3] The Draft Guidance applies to sponsors or applicants of products regulated by CDER and CBER who engage in formal meetings with FDA.[4] It does not apply to Abbreviated New Drug Applications (ANDAs), applications for biosimilar biological products, or submissions for medical devices.[5] Additionally, with the publication of the Draft Guidance, FDA withdrew two prior guidance documents: "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products" (published December 2017) and "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products" (published June 2018).[6]

Notable revisions in the Draft Guidance include new formal Type D Meetings and Initial Targeted Engagement for Regulatory Advice on CDER and CBER Products (INTERACT) Meetings, the recategorization of meeting formats, and the formal opportunity to request clarification or follow-up correspondence after meetings.[7]

This Client Alert analyzes the Draft Guidance and contextualizes it within FDA's recent initiatives to engage with stakeholders following the industry's negotiations with FDA that were reflected by Agency mandates in recent user fee bills.

Background

PDUFA VII

On September 30, 2022, President Biden signed the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023, which reauthorized PDUFA VII.[8] (Read this Latham Client Alert for more information.) PDUFA VII contains the terms by which FDA can collect user fees related to prescription drugs and biologic products through Fiscal Year 2027.[9] In its PDUFA VII commitment letter, FDA agreed to establish Type D Meetings and INTERACT Meetings and to formalize the process for sponsors to submit clarifying questions on formal meetings.[10] FDA also established various meeting management performance goals for both existing and new meeting types.[11] The Draft Guidance explains the procedures for existing formal meeting types and describes the new formal meeting types and procedures, which may lead to improved interactions with stakeholders.

Overview of Existing Formal Meeting Types

Several types of formal meetings between PDUFA sponsors and FDA occurred before PDUFA VII and continued after its reauthorization. The Draft Guidance includes FDA's current descriptions of the four existing formal meeting types that have been and continue to be available to PDUFA sponsors and applicants. Below is a brief overview of each meeting type.

- **Type A Meeting.** A sponsor or applicant can request a Type A meeting when a meeting is "necessary for an otherwise stalled product development program to proceed or to address an important safety issue."[12] A Type A meeting might be held for a dispute resolution proceeding, to discuss clinical holds, or as a "post-action meeting [that is] requested within three months of an FDA regulatory action other than an approval," among other reasons.[13]

- **Type B Meeting.** A sponsor or applicant can request a Type B meeting to discuss pre-investigational new drug applications, pre-emergency authorizations, pre-new drug applications, pre-biologics license applications, risk evaluation or mitigation strategies, post-marketing requirements, and other topics.[14]

- **Type B End-of-Phase Meeting.** A sponsor or applicant can request a Type B end-of-phase meeting to discuss matters that arise at the end of Phases 1 and 2 of a product's development program.[15]

- **Type C Meeting.** A catch-all category, a sponsor or applicant can request a Type D meeting for anything other than the topics discussed during the other meeting types "regarding the development and review of a product."[16] An example of a Type C Meeting is a meeting to "facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use."[17]

The Draft Guidance

The Draft Guidance introduces the following notable revisions from previous versions of the guidance document: explanations of two new formal meeting types, recategorization of meeting formats, and a formalized process for submitting "Requests for Clarification."[18]

New Formal Meeting Types

- **Type D Meeting.** A sponsor or applicant can request a Type D meeting to "discuss issues at key decision points to provide timely feedback critical to move the program forward."[19] The meeting must focus on a "narrow set of issues," such as a "narrow issue on which the sponsor is seeking Agency input with only a few (e.g., three to five questions total) associated questions," or a "general question about an innovative development approach that does not require detailed, extensive advice."[20] Additionally, the meeting should cover no more than "two focused topics"[21] and may not be the appropriate meeting type if a sponsor's or applicant's question is broad or requires "input from more than three disciplines or divisions."[22] In the Draft Guidance, FDA provides examples of specific questions that are appropriate for a Type D meeting, including questions about part of a complicated or innovative trial design, questions about data presentation after a pre-BLA/NDA meeting, and follow-up questions that result from a Type C meeting.[23] If a sponsor or applicant would like to discuss more than two narrow topics or one highly complicated issue that has various sub-questions or requires cross-center review, the sponsor or applicant should request a Type C meeting.[24] If FDA determines that a Type D meeting request is not appropriate, the Agency would convert the request into the appropriate meeting type and inform the sponsor.[25] The sponsor or applicant can then either accept the new meeting type or withdraw the original request.[26]

- **INTERACT Meeting.** A sponsor or applicant can request an INTERACT meeting to discuss topics related to "unique challenges in early development" related to "novel products and development programs."[27] FDA defines "early development" as any time before a pre-investigational new drug (IND) meeting or before filing an IND.[28] The Agency intends to use INTERACT meetings to provide early input that would help sponsors resolve "challenging" issues that might otherwise "delay progress of the product towards entry into the clinic."[29] As such, issues discussed at INTERACT Meetings should involve some aspect of IND requirements.[30] FDA provides several examples of topics appropriate for an INTERACT Meeting. They include pre-IND issues such as choosing appropriate preclinical models, designing proof-of-concept or other pilot safety/biodistribution studies necessary to a first-in-human clinical trial, and navigating a future first-in-human trial in a novel target clinical population for which there is no guidance.[31] Notably, a sponsor or applicant cannot request an INTERACT meeting unless they "have selected a specific investigational product or a product-derivation strategy to evaluate in a clinical study."[32]

Recategorized Meeting Formats

In the Draft Guidance, FDA recategorizes meeting formats to include virtual meetings in the "face-to-face" meeting category instead of the purely "teleconference/videoconference" category in the prior version of the draft guidance.[33] There are now four meeting formats: in person face-to-face, virtual face-to-face, teleconference, and Written Response Only (WRO).[34] FDA advises that individuals who are core attendees at meetings participate in person, if possible.[35] Otherwise, core attendees and other individuals can participate virtually.[36] Additionally, if core attendees do not plan to participate in person, a sponsor or applicant should initially request a virtual face-to-face meeting.[37]

Formalized Process for Clarifying Questions

The Draft Guidance also establishes a formalized process for sponsors and applicants to ask clarifying questions during all meeting types. Within 20 calendar days after a formal meeting or receipt of a WRO, sponsors may send clarifying questions in writing to the Agency as a "Request for Clarification."[38]

FDA notes that the questions must be of a "clarifying nature" and should not raise new issues.[39] FDA intends to issue a response to any properly asked "Request for Clarification" within 20 calendar days.[40]

Other FDA Initiatives to Interact With Stakeholders

In addition to the Draft Guidance, FDA published several other new or revised guidance documents in FY 2023 regarding interactions between FDA and industry stakeholders, including developers or manufacturers of generic drug products, biosimilar products, and medical devices. These guidance documents include the following:

- In September 2023, in connection with the Generic Drug User Fee Amendments (GDUFA) of 2022, as described in the "GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023-2027,"[41] FDA published a new draft guidance titled "Post-Warning Letter Meetings Under GDUFA."[42] This new draft guidance describes the Agency's proposed process for scheduling Post-Warning Letter Meetings between manufacturers of generic drugs after an FDA inspection has been classified as "Official Action Indicated," a manufacturer has received a Warning Letter from FDA regarding Current Good Manufacturing Practice compliance issues, and the manufacturer has responded to the Warning Letter.

- In August 2023, FDA updated its June 2018 draft guidance, "Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products,"[43] to align with FDA's Biosimilar User Fee Act (BsUFA) III goals as described in the "Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027."[44] This revised draft guidance provides, among other things, clarification on the data expectations pertaining to Biosimilar Initial Advisory meeting requests, the addition of Biological Product Development (BPD) Type 2a meetings, and changes to when the meeting background package is submitted for BPD Type 4 meetings.

- In June 2023, FDA updated its January 2021 guidance, "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program,"[45] to align the guidance with the Agency's performance goals described in the Medical Device User Fee Amendments of 2022 (MDUFA V) commitment letter.[46] This FDA guidance describes the several types of interactions or meetings that the medical device industry may request, including, Pre-Submissions, Submission Issue Requests, Study Risk Determinations, and Information Meetings.

- In February 2023, pursuant to FDA's GDUFA III commitments, the Agency issued the draft guidance, "Product-Specific Guidance Meetings Between FDA and ANDA Applicants Under GDUFA."[47] This draft guidance aims to provide the generic drug industry with recommendations on product-specific guidance meetings between FDA and the applicant who has submitted an ANDA.

- In October 2022, the Agency revised its guidance, "Formal Meetings Between FDA and ANDA Applicants of Complex products Under GDUFA."[48] This guidance was updated to align with FDA's GDUFA III commitment letter and includes information on complex product meeting types, including Mid-Cycle Review Meetings, Enhanced Mid-Cycle Review Meetings, and post-complete response letter scientific meetings.

Conclusions

The Draft Guidance expands opportunities for industry to meet with FDA, reflecting the terms that FDA and industry stakeholders agreed to during PDUFA VII negotiations. Specifically, the Draft Guidance provides PDUFA sponsors and applicants with additional meeting types, reorganizes the formats of meetings, and

provides opportunities to ask clarifying questions when interacting with the Agency regarding a meeting. In addition to these changes, FDA has also increased options for interaction between the Agency and other stakeholders through recent updates to other draft and final guidance documents.

These opportunities to interact with FDA result from industry's ongoing negotiations with FDA on user fee provisions. As PDUFA sponsors and applicants and other industry stakeholders use these opportunities to interact with the Agency, FDA may publish more guidance regarding these interactions and other opportunities to work directly and indirectly with the industry stakeholders it regulates.

Interested parties may submit written or electronic comments regarding the Draft Guidance by December 21, 2023.[49]

If you have questions about this Client Alert, please contact one of the authors listed below or the Latham lawyer with whom you normally consult:

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Endnotes

[1] See FDA, Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products (Sept. 2023), https://www.fda.gov/media/172311/download.

[2] Latham & Watkins, Client Alert: Continuing Appropriations Act Includes FDA Reauthorization of User Fees (Oct. 4, 2022), https://www.lw.com/admin/upload/SiteAttachments/Alert-3016.pdf.

[3] FDA, supra note 1, at 1 n.1.

[4] Id. at 1.

[5] Id.

[6] Id. at 1 n.2.

[7] Formal Meetings Between the Food and Drug Administration and Sponsors or Applicants of Prescription Drug User Fee Act Products; Draft Guidance for Industry; Availability, 88 Fed. Reg. 65,395, 65,396 (Sept. 22, 2023).

[8] Latham & Watkins, supra note 2.

[9] Id.

[10] See id.; FDA, PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027, https://www.fda.gov/media/151712/download (last visited Oct. 2, 2023).

[11] See FDA, supra note 10, at 24.

[12] FDA, supra note 1, at 2.

[13] Id. at 2–3.

[14] Id. at 3.

[15] Id. at 3–4.

[16] Id. at 4.

[17] Id.

[18] 88 Fed. Reg. 65,395, 65,396 (Sept. 22, 2023).

[19] Id.

[20] Id.

[21] Id.

[22] Id.

[23] Id. at 4–5.

[24] Id. at 4.

[25] Id.

[26] Id.

[27] Id. at 5.

[28] Id.

[29] Id.

[30] Id.

[31] Id.

[32] Id.

[33] Id. at 6.; FDA, Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products (Dec. 2017), https://www.fda.gov/media/109951/download.

[34] FDA, supra note 1, at 6.

[35] Id.

[36] Id.

[37] Id.

[38] Id. at 18.

[39] Id.

[40] Id.

[41] See FDA, GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023-2027, https://www.fda.gov/media/153631/download.

[42] See FDA, Post-Warning Letter Meetings Under GDUFA (Sept. 2023), https://www.fda.gov/media/171785/download.

[43] See FDA, Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products (Aug. 2023), https://www.fda.gov/media/113913/download.

[44] See FDA, Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027, https://www.fda.gov/media/152279/download.

[45] See FDA, Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program (June 2, 2023), https://www.fda.gov/media/114034/download.

[46] See FDA, MDUFA Performance Goals and Procedures, Fiscal Years 2023 Through 2027, https://www.fda.gov/media/158308/download.

[47] See FDA, Product-Specific Guidance Meetings Between FDA and ANDA Applicants Under GDUFA (Feb. 2023), https://www.fda.gov/media/165468/download.

[48] See FDA, Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA, Revision 1 (Oct. 2022), https://www.fda.gov/media/107626/download.

[49] 88 Fed. Reg. 65,395, 65,396 (Sept. 22, 2023).